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FILE 'HOME' ENTERED AT 11:31:18 ON 16 AUG 2002

=> index bioscience agriculture chemistry patents medicine
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         3.99       3.99

INDEX 'ADISALERTS, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI,
       BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA,
       CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB,
       DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...'
ENTERED AT 11:42:30 ON 16 AUG 2002

102 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s (antimicrobial (w) peptide ) and (lentiviral (w) lytic (w) peptides)
          1   FILE BIOSIS
  22 FILES SEARCHED...
  39 FILES SEARCHED...
  64 FILES SEARCHED...
  94 FILES SEARCHED...

   1 FILES HAVE ONE OR MORE ANSWERS,  102 FILES SEARCHED IN STNINDEX

L1   QUE (ANTIMICROBIAL (W) PEPTIDE ) AND (LENTIVIRAL (W) LYTIC (W) PEPTIDES)

=> file hits
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         2.12       6.11

FILE 'BIOSIS' ENTERED AT 11:45:09 ON 16 AUG 2002
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CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 14 August 2002 (20020814/ED)


=> s l1
         32093 ANTIMICROBIAL
          2738 ANTIMICROBIALS
         33547 ANTIMICROBIAL
                 (ANTIMICROBIAL OR ANTIMICROBIALS)
        215757 PEPTIDE
        108344 PEPTIDES
        274764 PEPTIDE
                 (PEPTIDE OR PEPTIDES)
          1514 ANTIMICROBIAL (W) PEPTIDE
           710 LENTIVIRAL
         11630 LYTIC
            10 LYTICS
         11637 LYTIC
                 (LYTIC OR LYTICS)
        108344 PEPTIDES
             2 LENTIVIRAL (W) LYTIC (W) PEPTIDES
L2           1 (ANTIMICROBIAL (W) PEPTIDE ) AND (LENTIVIRAL (W) LYTIC (W) PEPTI
               DES)
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=> d l2 ibib abs

L2 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:176245 BIOSIS
DOCUMENT NUMBER: PREV200200176245
TITLE: Antibacterial activity of engineered **lentiviral lytic peptides**.
AUTHOR(S): Mietzner, T. A. (1); Phadke, S. M. (1); Kapoor, S. A. (1); Pelinkovik, D. (1); Montelaro, R. C. (1)
CORPORATE SOURCE: (1) University of Pittsburgh School of Medicine, Pittsburgh, PA USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 33. http://www.asmusa.org/mtgsrc/generalmeeting.htm. print. Meeting Info.: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001 ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Background: The lentivirus lytic peptides are cationic **antimicrobial peptides** derived from the C-terminus of the HIV1 gp41. The 28-residue parent peptide (LLP1) is structurally similar to human cathelicidin (LL37) but compositionally unique. Engineered LLPs (eLLPs) were derived from amino acid substitutions of LLP1, optimizing charge and length. This study evaluates the in vitro eLLP activity and mechanism of action and eLLP in vivo activity using a septic rabbit joint model. Methods and Results: Using a standard solution phase assay, we demontrate eLLPs to be as, or more, active than other membrane-active **antimicrobial peptides** such as LL37 or polymyxin when tested against Staphylococcus aureus or Pseudomonas aeruginosa (MBC=0.1-3.0 mM). The eLLPs are active under physiologic conditions (150mM NaCl) and one Trp-rich eLLP showed impressive activity against multiple genomovars of Burkholderia cepacia complex. The mechanism of eLLP action against gram-negative bacteria was investigated using well-accepted outer membrane (OM) and cytoplasmic membrane (CM) markers n-phenylnaphthaline and cytosolic b-galactosidase, respectively. Our findings indicate that eLLPs disrupt both the OM and CM, in contrast to polymyxin, which was poorly active against the OM. The eLLP activity was tested in a septic rabbit knee joint model using S. aureus as a test organism. Lavaging the infected joint with 100muM eLLP significantly decreased the bacterial load in the joint and was equally effective as standard treatment with 1.4% neomycin. When both eLLP and neomycin were given together a maximal decrease in bacterial load was observed, however in no case was the joint completely sterilized. In control experiments minimal toxicity associated with peptide treatment was observed. Conclusion: The eLLPs show promise as antimicrobial compounds for the treatment of infections associated with confined compartments.

=> s antimicrobial and (lentiviral (w) lytic (w) peptides)
32093 ANTIMICROBIAL
2738 ANTIMICROBIALS
33547 ANTIMICROBIAL
(ANTIMICROBIAL OR ANTIMICROBIALS)
710 LENTIVIRAL
11630 LYTIC
10 LYTICS
11637 LYTIC
(LYTIC OR LYTICS)
108344 PEPTIDES
2 LENTIVIRAL (W) LYTIC (W) PEPTIDES
L3 2 ANTIMICROBIAL AND (LENTIVIRAL (W) LYTIC (W) PEPTIDES)

=> d l3 1-2 ibib abs

L3 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:176245 BIOSIS
DOCUMENT NUMBER: PREV200200176245
TITLE: Antibacterial activity of engineered **lentiviral lytic peptides**.
AUTHOR(S): Mietzner, T. A. (1); Phadke, S. M. (1); Kapoor, S. A. (1); Pelinkovik, D. (1); Montelaro, R. C. (1)
CORPORATE SOURCE: (1) University of Pittsburgh School of Medicine, Pittsburgh, PA USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 33. http://www.asmusa.org/mtgsrc/generalmeeting.htm. print. Meeting Info.: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001 ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Background: The lentivirus lytic peptides are cationic **antimicrobial** peptides derived from the C-terminus of the HIV1 gp41. The 28-residue parent peptide (LLP1) is structurally similar to human cathelicidin (LL37) but compositionally unique. Engineered LLPs (eLLPs) were derived from amino acid substitutions of LLP1, optimizing charge and length. This study evaluates the in vitro eLLP activity and mechanism of action and eLLP in vivo activity using a septic rabbit joint model. Methods and Results: Using a standard solution phase assay, we demontrate eLLPs to be as, or more, active than other membrane-active **antimicrobial** peptides such as LL37 or polymyxin when tested against Staphylococcus aureus or Pseudomonas aeruginosa (MBC=0.1-3.0 mM). The eLLPs are active under physiologic conditions (150mM NaCl) and one Trp-rich eLLP showed impressive activity against multiple genomovars of Burkholderia cepacia complex. The mechanism of eLLP action against gram-negative bacteria was investigated using well-accepted outer membrane (OM) and cytoplasmic membrane (CM) markers n-phenylnaphthaline and cytosolic b-galactosidase, respectively. Our findings indicate that eLLPs disrupt both the OM and CM, in contrast to polymyxin, which was poorly active against the OM. The eLLP activity was tested in a septic rabbit knee joint model using S. aureus as a test organism. Lavaging the infected joint with 100muM eLLP significantly decreased the bacterial load in the joint and was equally effective as standard treatment with 1.4% neomycin. When both eLLP and neomycin were given together a maximal decrease in bacterial load was observed, however in no case was the joint completely sterilized. In control experiments minimal toxicity associated with peptide treatment was observed. Conclusion: The eLLPs show promise as **antimicrobial** compounds for the treatment of infections associated with confined compartments.

L3 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:9311 BIOSIS
DOCUMENT NUMBER: PREV200100009311
TITLE: **Antimicrobial** activity of lentivirus lytic peptide derivatives in cystic fibrosis airway infection and septic arthritis.
AUTHOR(S): Phadke, S. M. (1); Kapoor, S. A. (1); Pelinkovic, D.; Montelaro, R. C.; Mietzner, T. A.
CORPORATE SOURCE: (1) Children's Hosp. of Pittsburgh, Pittsburgh, PA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2000) Vol. 40, pp. 232. print. Meeting Info.: 40th Interscience Conference on Antimicrobial Agents and Chemotherapy Toronto, Ontario, Canada September 17-20, 2000
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

```
=> s (antimicrobial (w) peptide ) and dimer and disulfide
         32093 ANTIMICROBIAL
          2738 ANTIMICROBIALS
         33547 ANTIMICROBIAL
                 (ANTIMICROBIAL OR ANTIMICROBIALS)
        215757 PEPTIDE
        108344 PEPTIDES
        274764 PEPTIDE
                 (PEPTIDE OR PEPTIDES)
          1514 ANTIMICROBIAL (W) PEPTIDE
         22898 DIMER
         13023 DIMERS
         31688 DIMER
                 (DIMER OR DIMERS)
         23492 DISULFIDE
          1992 DISULFIDES
         24303 DISULFIDE
                 (DISULFIDE OR DISULFIDES)
L4           2 (ANTIMICROBIAL (W) PEPTIDE ) AND DIMER AND DISULFIDE

=> d l4 1-2 ibib abs

L4   ANSWER 1 OF 2  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER:   1996:364454  BIOSIS
DOCUMENT NUMBER:    PREV199699086810
TITLE:              Purification and structural characterization of bovine
                    cathelicidins, precursors of antimicrobial
                    peptides.
AUTHOR(S):          Storici, Paola; Tossi, Alessandro; Lenarcic, Brigita;
                    Romeo, Domenico (1)
CORPORATE SOURCE:   (1) Dip. Biochim. Biofis. Chim. Macromol., Univ. Trieste,
                    via L. Giorgieri, I-34127 Trieste Italy
SOURCE:             European Journal of Biochemistry, (1996) Vol. 238, No. 3,
                    pp. 769-776.
                    ISSN: 0014-2956.
DOCUMENT TYPE:      Article
LANGUAGE:           English
AB   Cathelicidins are a novel family of antimicrobial
     peptide precursors from mammalian myeloid cells. They are
     characterized by a conserved N-terminal region while the C-terminal
     antimicrobial domain can vary considerably in both primary sequence and
     length. Four cathelicidins, proBac5, proBac7, prododecapeptide and
     proBMAP-28, have been concurrently purified from bovine neutrophils, using
     simple and rapid methodologies. The correlation of ES-MS data from the
     purified proteins with their cDNA-deduced sequences has revealed several
     common features of their primary sequence, such as the presence of
     N-terminal 5-oxoproline (pyroglutamate) residues and two disulfide
     bridges in a 1-2, 3-4 arrangement. The N-terminal domains of the
     cathelicidins present one or two Asp-Pro bonds, which are particularly
     acid-labile in proBac5 and proBac7, but stable in prododecapeptide. This
     suggests that the spatial organization around these bonds may vary in
     different cathelicidins, and favour hydrolysis in some cases. An
     unexpected feature of the prododecapeptide is that it exists as
     dimers formed by three possible combinations of its two isoforms.
     The isolation of a truncated, monomeric form of this protein, lacking the
     cysteine-containing antimicrobial dodecapeptide, indicates that
     dimerization occurs via disulfide bridge formation at the level
     of the C-terminal domain and that the dodecapeptide is likely released as
     a dimer from its precursor. Sequence-based secondary structure
     predictions and CD results indicate for cathelicidins a 30-50% content of
     extended conformation and lt 20% content of alpha-helical conformation,
     with the alpha-helical segment placed near the N-terminus. Finally,
     similarity searching and topology-based structure prediction underline a
     significant sequential and structural similarity between the conserved
     N-terminal domain of cathelicidins and cystatin-like domains, placing this
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family within the cystatin superfamily. When assayed against cathepsin L, unlike the potent cystatin inhibitors, three of the four cathelicidins show only a poor inhibitory activity (K-i = 0.6-3 mu-M).

L4 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:147461 BIOSIS
DOCUMENT NUMBER: BA93:81686
TITLE: ISOLATION AND CHARACTERIZATION OF A NOVEL CLASS OF PLANT **ANTIMICROBIAL PEPTIDES** FROM MIRABILIS-JALAPA L. SEEDS.
AUTHOR(S): CAMMUE B P A; DE BOLLE M F C; TERRAS F R G; PROOST P; VAN DAMME J; REES S B; VANDERLEYDEN J; BROEKAERT W F
CORPORATE SOURCE: F.A. JANSSENS LAB. GENETICS, CATHOLIC UNIVERSITY LEUVEN, WILLEM DE CROYLAAN 42, B-3001 HEVERLEE, BELGIUM.
SOURCE: J BIOL CHEM, (1992) 267 (4), 2228-2233.
CODEN: JBCHA3. ISSN: 0021-9258.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB We have isolated from seeds of Mirabilis jalapa L. two **antimicrobial peptides**, designated Mj-AMP1 and Mj-AMP2, respectively. These peptides are highly basic and consist of 37 and 36 residues for Mj-AMP1 and Mj-AMP2, respectively. Both peptides contain three **disulfide** bridges and differ from one another only by 4 amino acids. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis analysis of the reduced and unreduced peptides suggests that the peptides associate into **dimers** in their native form. The Mj-AMPs exhibit a broad spectrum of antifungal activity since they are active against all 13 tested plant pathogenic fungi. Concentrations required for 50% inhibition of fungal growth vary from 6 to 300 .mu.g/ml for Mj-AMP1 and from 0.5 to 20 .mu.g/ml for Mj-AMP2. These peptides were also active on two tested Gram-positive bacteria but were apparently nontoxic for Gram-negative bacteria and cultured human cells. Although the Mj-AMPs show sequence similarity to .mu.-agatoxins, a class of insecticidal neurotoxic peptides isolated from the venom of spiders, they do not affect pulse transmission in insect nerves.

```
=> (antimicrobial (w) peptide ) and adminstering and parenterally
(ANTIMICROBIAL IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s (antimicrobial (w) peptide ) and adminstering and parenterally
         32093 ANTIMICROBIAL
          2738 ANTIMICROBIALS
         33547 ANTIMICROBIAL
                 (ANTIMICROBIAL OR ANTIMICROBIALS)
        215757 PEPTIDE
        108344 PEPTIDES
        274764 PEPTIDE
                 (PEPTIDE OR PEPTIDES)
          1514 ANTIMICROBIAL (W) PEPTIDE
            16 ADMINSTERING
          2503 PARENTERALLY
L5           0 (ANTIMICROBIAL (W) PEPTIDE ) AND ADMINSTERING AND PARENTERALLY

=> s (antimicrobial (w) peptide ) and (solid (w) phase)
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          2738 ANTIMICROBIALS
         33547 ANTIMICROBIAL
                 (ANTIMICROBIAL OR ANTIMICROBIALS)
        215757 PEPTIDE
        108344 PEPTIDES
        274764 PEPTIDE
```

(PEPTIDE OR PEPTIDES)
1514 ANTIMICROBIAL (W) PEPTIDE
85711 SOLID
15524 SOLIDS
99349 SOLID
(SOLID OR SOLIDS)
335309 PHASE
59038 PHASES
366608 PHASE
(PHASE OR PHASES)
25648 SOLID (W) PHASE
L6 26 (ANTIMICROBIAL (W) PEPTIDE ) AND (SOLID (W) PHASE)

=> d l6 1-24 ibib abs

L6 ANSWER 1 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:338731 BIOSIS
DOCUMENT NUMBER: PREV200200338731
TITLE: Structural requirements for potent versus selective cytotoxicity for antimicrobial dermaseptin S4 derivatives.
AUTHOR(S): Kustanovich, Irina (1); Shalev, Deborah E.; Mikhlin, Masha; Gaidukov, Leonid; Mor, Amram
CORPORATE SOURCE: (1) Dept. of Biological Chemistry, Institute of Life Sciences, Hebrew University of Jerusalem, Givat Ram, 91904, Jerusalem: irinak@macbeth.ls.huji.ac.il Israel
SOURCE: Journal of Biological Chemistry, (May 10, 2002) Vol. 277, No. 19, pp. 16941-16951. http://www.jbc.org/. print. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
AB To better understand the structural requirements for selective cytotoxicity of **antimicrobial peptides**, seven dermaseptin S4 analogs were produced and investigated with respect to molecular organization in solution, binding properties to model phospholipid membranes, and cytotoxic properties. Native dermaseptin S4 displayed high aggregation in solution and high binding affinity. These properties correlated with high cytotoxicity. Yet, potency was progressively limited when facing cells whose plasma membrane was surrounded by increasingly complex barriers. Increasing the positive charge of the native peptide led to partial depolymerization that correlated with higher binding affinity and with virtually non-discriminative high cytotoxicity against all cell types. The C-terminal hydrophobic domain was found responsible for binding to membranes but not for their disruption. Truncations of the C terminus combined with increased positive charge of the N-terminal domain resulted in short peptides having similar binding affinity as the parent compound but displaying selective activity against microbes with reduced toxicity toward human red blood cells. Nuclear magnetic resonance-derived three-dimensional structures of three active derivatives enabled the delineation of a common amphipathic structure with a clear separation of two lobes of positive and negative electrostatic potential surfaces. Whereas the spatial positive electrostatic potential extended considerably beyond the peptide dimensions and was required for potency, selectivity was affected primarily by hydrophobicity. The usefulness of this approach for the design of potent and/or selective cytolytic peptides is discussed herein.

L6 ANSWER 2 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:232258 BIOSIS
DOCUMENT NUMBER: PREV200200232258
TITLE: Peptides with indirect in vivo activity against an intracellular pathogen: Selective lysis of infected macrophages.
AUTHOR(S): Yokum, T. S.; Hammer, R. P.; McLaughlin, M. L. (1); Elzer, P. H.

CORPORATE SOURCE: (1) Department of Chemistry, Louisiana State University, Baton Rouge, LA, 70803: mmclaug@lsu.edu USA
SOURCE: Journal of Peptide Research, (January, 2002) Vol. 59, No. 1, pp. 9-17. http://journals.munksgaard.dk/peptideresearch. print.
ISSN: 1397-002X.
DOCUMENT TYPE: Article
LANGUAGE: English

AB A collection of natural peptides, simplified analogs of natural peptides, de novo amphipathic peptides and de novo amphipathic peptides composed of 50-80% alpha,alpha-dialkylated glycines (alpha,alpha-Dags) were synthesized on **solid-phase** resin as the C-terminus amides using N-alpha-fluorenylmethyloxycarbonyl protection. The synthesis of the peptides rich in alpha,alpha-Dags used acid fluoride coupling methods. The peptides show antimicrobial activity against Escherichia coli and Staphylococcus aureus but no direct antimicrobial activity against Brucella abortus at 100 muM in vitro. However, in vivo treatment with several of these peptides results in significant reductions of B. abortus in chronically infected immune BALB/c mice relative to infected control animals. The chronically infected mice were susceptible to peptide toxicity at much lower peptide doses than control animals. The highest nonlethal dose for infected mice was only 25 mug for melittin, whereas 500 mug doses were nonlethal for many of the other peptides. Several of the alpha,alpha-Dag-rich peptides selectively destroy B. abortus-infected murine macrophages in vitro. Thus, these peptides apparently reduce the bacterial load in vivo by destroying a portion of the infected macrophages and exposing the sequestered bacteria to the immune response in the mice.

L6 ANSWER 3 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:216205 BIOSIS
DOCUMENT NUMBER: PREV200200216205
TITLE: Chemoenzymatic synthesis of peptidyl 3,4-dihydroxyphenylalanine for structure-activity relationships in marine invertebrate polypeptides.
AUTHOR(S): Taylor, Steven W. (1)
CORPORATE SOURCE: (1) Center for Marine Biotechnology and Biomedicine, Scripps Institution of Oceanography, University of California, San Diego, La Jolla, CA, 92093-0204: swtaylor@ucsd.edu USA
SOURCE: Analytical Biochemistry, (March 1, 2002) Vol. 302, No. 1, pp. 70-74. http://www.academicpress.com/ab. print.
ISSN: 0003-2697.
DOCUMENT TYPE: Article
LANGUAGE: English

AB An improved method for hydroxylating tyrosine-containing sequences in polypeptides to peptidyl 3,4-dihydroxyphenylalanine (DOPA) using mushroom tyrosinase at relatively high enzyme-to-substrate ratios is described. The new method involves incorporating borate into the reaction mixture to stop formation of the unwanted side product 3,4,5-trihydroxyphenylalanine. Using this method, a model for the palindromic central sequence for the **antimicrobial peptide** family, the styelins, Y*Y*KHKY*Y* (where Y* is DOPA), was successfully synthesized in high yield from YYKHKYY. This sequence represents a particularly challenging target because of the cluster of four precursor tyrosine residues are in close proximity. The method should be readily applied to larger polypeptides produced by either **solid-phase** synthesis or recombinant techniques and give greater insight into the roles of this unusual posttranslational modification in marine invertebrates such as mussels and ascidians.

L6 ANSWER 4 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:208983 BIOSIS
DOCUMENT NUMBER: PREV200200208983
TITLE: Retrocyclin: A primate peptide that protects cells from infection by T- and M-tropic strains of HIV-1.

AUTHOR(S): Cole, Alexander M.; Hong, Teresa; Boo, Lee Ming; Nguyen, Tung; Zhao, Chengquan; Bristol, Greg; Zack, Jerome A.; Waring, Alan J.; Yang, Otto O.; Lehrer, Robert I. (1)

CORPORATE SOURCE: (1) Department of Medicine, University of California School of Medicine, 10833 Le Conte Avenue, CHS 37-062, Los Angeles, CA, 90095: rlehrer@mednet.ucla.edu USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (February 19, 2002) Vol. 99, No. 4, pp. 1813-1818. http://www.pnas.org. print. ISSN: 0027-8424.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Human bone marrow expresses a pseudogene that encodes an **antimicrobial peptide** homologous to rhesus monkey circular minidefensins (theta-defensins). We prepared the putative ancestral human peptide by **solid-phase** synthesis and named it "retrocyclin." Retrocyclin did not cause direct inactivation of HIV-1, and its modest antibacterial properties resembled those of its rhesus homologs. Nevertheless, retrocyclin had a remarkable ability to inhibit proviral DNA formation and to protect immortalized and primary human CD4+ lymphocytes from in vitro infection by both T-tropic and M-tropic strains of HIV-1. Confocal fluorescent microscopy studies performed with BODIPY-FL-labeled RC-101, a close analog of retrocyclin, showed that the peptide formed patch-like aggregates on the surface of CD4+ cells. These findings suggest that retrocyclin interferes with an early stage of HIV-1 infection and that retrocyclin-like agents might be useful topical agents to prevent sexually acquired HIV-1 infections.

L6 ANSWER 5 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:97031 BIOSIS

DOCUMENT NUMBER: PREV200200097031

TITLE: Anoplin, a novel **antimicrobial peptide** from the venom of the solitary wasp Anoplius samariensis.

AUTHOR(S): Konno, Katsuhiro (1); Hisada, Miki; Fontana, Renato; Lorenzi, Carla C. B.; Naoki, Hideo; Itagaki, Yasuhiro; Miwa, Akiko; Kawai, Nobufumi; Nakata, Yoshihiro; Yasuhara, Tadashi; Ruggiero Neto, Joao; de Azevedo Junior, Walter F.; Palma, Mario S.; Nakajima, Terumi

CORPORATE SOURCE: (1) Center of Study of Social Insects, Department of Biology, Institute of Biosciences of Rio Claro, Sao Paulo State University, Av. 24-A, 1515, Rio Claro, SP, 13506-900: kk-gon@rc.unesp.br Brazil

SOURCE: Biochimica et Biophysica Acta, (26 November, 2001) Vol. 1550, No. 1, pp. 70-80. print. ISSN: 0006-3002.

DOCUMENT TYPE: Article

LANGUAGE: English

AB A novel **antimicrobial peptide**, anoplin, was purified from the venom of the solitary wasp Anoplius samariensis. The sequence was mostly analyzed by mass spectrometry, which was corroborated by **solid-phase** synthesis. Anoplin, composed of 10 amino acid residues, Gly-Leu-Leu-Lys-Arg-Ile-Lys-Thr-Leu-Leu-NH2, has a high homology to crabrolin and mastoparan-X, the mast cell degranulating peptides from social wasp venoms, and, therefore, can be predicted to adopt an amphipathic alpha-helix secondary structure. In fact, the circular dichroism (CD) spectra of anoplin in the presence of trifluoroethanol or sodium dodecyl sulfate showed a high content, up to 55%, of the alpha-helical conformation. A modeling study of anoplin based on its homology to mastoparan-X supported the CD results. Biological evaluation using the synthetic peptide revealed that this peptide exhibited potent activity in stimulating degranulation from rat peritoneal mast cells and broad-spectrum antimicrobial activity against both Gram-positive and Gram-negative bacteria. Therefore, this is the first antimicrobial component to be found in the solitary wasp venom and it may play a key role in preventing potential infection by microorganisms during

prey consumption by their larvae. Moreover, this peptide is the smallest among the linear alpha-helical **antimicrobial peptides** hitherto found in nature, which is advantageous for chemical manipulation and medical application.

L6 ANSWER 6 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:40702 BIOSIS
DOCUMENT NUMBER: PREV200200040702
TITLE: Chemical synthesis, molecular modeling, and antimicrobial activity of a novel bacteriocin, MMFII.
AUTHOR(S): Ferchichi, Mounir; Fathallah, Mohamed; Mansuelle, Pascal; Rochat, Herve; Sabatier, Jean-Marc; Manai, Mohamed (1); Mabrouk, Kamel
CORPORATE SOURCE: (1) Laboratoire de Biochimie et Biologie Moleculaire, Departement de Biologie, Faculte des Sciences de Tunis, El Manar, 2092, Tunis: mohamedmanai@yahoo.fr, mbrouk.k@jean-roche.univ-mrs.fr Tunisia
SOURCE: Biochemical and Biophysical Research Communications, (November 23, 2001) Vol. 289, No. 1, pp. 13-18. print. ISSN: 0006-291X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB A new **antimicrobial peptide**, referred to as MMFII, was purified to homogeneity from lactic acid bacteria Lactococcus lactis, which were isolated from Tunisian dairy product. The complete amino acid sequence of the peptide has been established by amino acid analysis, Edman sequencing, and mass spectrometry and verified by **solid-phase** chemical synthesis. MMFII is a single-chain 37-residue polypeptide containing a single intramolecular disulfide bond, i.e., TSYGNGVHCNKSKCWIDVSELETYKAGTVSNPKDILW. It shares ca. 35% sequence identity with Leucocin A, a class IIa bacteriocin. Modeling based on the 3-D of Leucocin A shows three beta strands located in the N-terminal region (Thr1-Tyr3, Val7-Asn10, Lys13-Ile16) and an alpha helical domain from Asp17 to Asn31. When plotted as an alpha-helical wheel, the central alpha-helix of MMFII does not exhibit an amphipathic helical structure. The synthetic MMFII (sMMFII), obtained by the **solid-phase** method, was shown to be indistinguishable from the natural peptide, sMMFII is active against Lactococcus cremoris and Listeria ivanovii bacteria, whereas no activity was detected for any of the synthetic N-terminal truncated MMFII analogs Cys9-Trp37, Trp15-Trp37, and Val18-Trp37.

L6 ANSWER 7 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:262475 BIOSIS
DOCUMENT NUMBER: PREV200100262475
TITLE: Synthetic combinatorial libraries: An emerging approach toward the identification of novel antimicrobial agents.
AUTHOR(S): Blondelle, Sylvie E. (1)
CORPORATE SOURCE: (1) Department of Biochemistry/Microbiology, Torrey Pines Institute for Molecular Studies, 3550 General Atomics Court, San Diego, CA, 92121: sblondelle@tpims.org USA
SOURCE: Abstracts of Papers American Chemical Society, (2001) Vol. 221, No. 1-2, pp. AGFD 99. print.
Meeting Info.: 221st National Meeting of the American Chemical Society San Diego, California, USA April 01-05, 2001
ISSN: 0065-7727.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L6 ANSWER 8 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:231200 BIOSIS
DOCUMENT NUMBER: PREV200100231200
TITLE: Three-dimensional structure of RTD-1, a cyclic

antimicrobial defensin from rhesus macaque leukocytes.
AUTHOR(S): Trabi, Manuela; Schirra, Horst Joachim; Craik, David J. (1)
CORPORATE SOURCE: (1) Institute for Molecular Bioscience (Centre for Drug Design and Development), University of Queensland, Brisbane, QLD, 4072: d.craik@imb.uq.edu.au Australia
SOURCE: Biochemistry, (April 10, 2001) Vol. 40, No. 14, pp. 4211-4221. print.
ISSN: 0006-2960.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Most mammalian defensins are cationic peptides of 29-42 amino acids long, stabilized by three disulfide bonds. However, recently Tang et al. (1999, Science 286, 498-502) reported the isolation of a new defensin type found in the leukocytes of rhesus macaques. In contrast to all the other defensins found so far, rhesus theta defensin-1 (RTD-1) is composed of just 18 amino acids with the backbone cyclized through peptide bonds. Antibacterial activities of both the native cyclic peptide and a linear form were examined, showing that the cyclic form was 3-fold more active than the open chain analogue (Tang et al. (1999) Science 286, 498-502). To elucidate the three-dimensional structure of RTD-1 and its open chain analogue, both peptides were synthesized using **solid-phase** peptide synthesis and tert-butyloxycarbonyl chemistry. The structures of both peptides in aqueous solution were determined from two-dimensional 1H NMR data recorded at 500 and 750 MHz. Structural constraints consisting of interproton distances and dihedral angles were used as input for simulated-annealing calculations and water refinement with the program CNS. RTD-1 and its open chain analogue oRTD-1 adopt very similar structures in water. Both comprise an extended beta-hairpin structure with turns at one or both ends. The turns are well defined within themselves and seem to be flexible with respect to the extended regions of the molecules. Although the two strands of the beta-sheet are connected by three disulfide bonds, this region displays a degree of flexibility. The structural similarity of RTD-1 and its open chain analogue oRTD-1, as well as their comparable degree of flexibility, support the theory that the additional charges at the termini of the open chain analogue rather than overall differences in structure or flexibility are the cause for oRTD-1's lower antimicrobial activity. In contrast to numerous other **antimicrobial peptides**, RTD-1 does not display any amphiphilic character, even though surface models of RTD-1 exhibit a certain clustering of positive charges. Some amide protons of RTD-1 that should be solvent-exposed in monomeric beta-sheet structures show low-temperature coefficients, suggesting the possible presence of weak intermolecular hydrogen bonds.

L6 ANSWER 9 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:33277 BIOSIS
DOCUMENT NUMBER: PREV200100033277
TITLE: Interaction between heat shock proteins and **antimicrobial peptides**.
AUTHOR(S): Otvos, Laszlo, Jr. (1); O, Insug; Rogers, Mark E.; Consolvo, Patricia J.; Condie, Barry A.; Lovas, Sandor; Bulet, Philippe; Blaszczyk-Thurin, Magdalena
CORPORATE SOURCE: (1) Wistar Institute, 3601 Spruce Street, Philadelphia, PA, 19104: Otvos@wistar.upenn.edu USA
SOURCE: Biochemistry, (November 21, 2000) Vol. 39, No. 46, pp. 14150-14159. print.
ISSN: 0006-2960.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Drosocin, pyrrhocoricin, and apidaecin, representing the short (18-20 amino acid residues) proline-rich antibacterial peptide family, originally isolated from insects, were shown to act on a target bacterial protein in a stereospecific manner. Native pyrrhocoricin and one of its analogues

designed for this purpose protect mice from bacterial challenge and, therefore, may represent alternatives to existing antimicrobial drugs. Furthermore, this mode of action can be a basis for the design of a completely novel set of antibacterial compounds, peptidic or peptidomimetic, if the interacting bacterial biopolymers are known. Recently, apidaecin was shown to enter Escherichia coli and subsequently kill bacteria through sequential interactions with diverse target macromolecules. In this paper report, we used biotin- and fluorescein-labeled pyrrhocoricin, drosocin, and apidaecin analogues to identify biopolymers that bind to these peptides and are potentially involved in the above-mentioned multistep killing process. Through use of a biotin-labeled pyrrhocoricin analogue, we isolated two interacting proteins from E. coli. According to mass spectrometry, Western blot, and fluorescence polarization, the short, proline-rich peptides bound to DnaK, the 70-kDa bacterial heat shock protein, both in solution and on the **solid-phase**. GroEL, the 60-kDa chaperonin, also bound in solution. Control experiments with an unrelated labeled peptide showed that while binding to DnaK was specific for the antibacterial peptides, binding to GroEL was not specific for these insect sequences. The killing of bacteria and DnaK binding are related events, as an inactive pyrrhocoricin analogue made of all-D-amino acids failed to bind. The pharmaceutical potential of the insect antibacterial peptides is underscored by the fact that pyrrhocoricin did not bind to Hsp70, the human equivalent of DnaK. Competition assay with unlabeled pyrrhocoricin indicated differences in GroEL and DnaK binding and a probable two-site interaction with DnaK. In addition, all three antibacterial peptides strongly interacted with two bacterial lipopolysaccharide (LPS) preparations in solution, indicating that the initial step of the bacterial killing cascade proceeds through LPS-mediated cell entry.

L6 ANSWER 10 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:519695 BIOSIS
DOCUMENT NUMBER: PREV200000519695
TITLE: Evaluation of the metal binding properties of the histidine-rich **antimicrobial peptides** histatin 3 and 5 by electrospray ionization mass spectrometry.
AUTHOR(S): Brewer, Dyanne; Lajoie, Gilles (1)
CORPORATE SOURCE: (1) Department of Chemistry, University of Waterloo, Waterloo, ON, N2L 3G1 Canada
SOURCE: Rapid Communications in Mass Spectrometry, (2000) Vol. 14, No. 19, pp. 1736-1745. print.
ISSN: 0951-4198.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Electrospray ionization mass spectrometry (ESI-MS) was used to investigate metal ion interactions with salivary peptides histatin 3 (H3) and histatin 5 (H5). Conformational changes of these peptides in the presence of metal ions were studied using circular dichroism spectroscopy. H3 and H5 formed high affinity complexes with Cu2+ and Ni2+ and, to a lesser extent, with Zn2+. Both peptides show the potential for multiple binding sites for Cu2+ and Ni2+ and only a single strong binding site for Zn2+. The binding of a third Cu2+ ion to H3 seems to enable the binding of a fourth ion to H3. The binding of a second and third Ni2+ ion to H5 has a similar effect in enabling the binding of a fourth ion. None of the metal ions examined stabilized a regular secondary structure for either peptide. Subtle changes in overall conformation are seen with the addition of Cu2+ to both H3 and H5.

L6 ANSWER 11 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:445388 BIOSIS
DOCUMENT NUMBER: PREV200000445388
TITLE: Development of protegrins for the treatment and prevention of oral mucositis: Structure-activity relationships of

synthetic protegrin analogues.
AUTHOR(S): Chen, Jie; Falla, Timothy J.; Liu, Hongjian; Hurst, Malinda A.; Fujii, Craig A.; Mosca, Deborah A.; Embree, Jay R.; Loury, David J.; Radel, Peggy A.; Chang, Conway Cheng; Gu, Leo; Fiddes, John C. (1)
CORPORATE SOURCE: (1) IntraBiotics Pharmaceuticals, Inc., 1255 Terra Bella Avenue, Mountain View, CA, 94043 USA
SOURCE: Biopolymers, (2000) Vol. 55, No. 1, pp. 88-98. print.
ISSN: 0006-3525.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Protegrin **antimicrobial peptides** possess activity against gram-positive and gram-negative bacteria and yeasts. An extensive structure-activity relationship (SAR) study was conducted on several hundred protegrin analogues to gain understanding of the relationship between the primary and secondary structure of the protegrins and their antimicrobial activities, and to identify a protegrin analogue for clinical development. Native sequence protegrins are cationic, amphiphilic peptides that are characterized by the presence of a beta-sheet structure that is maintained by two disulfide bridges. The presence of the beta-sheet is key to the stability of the protegrin structure; linearized analogues or analogues that have amino acid substitutions that eliminate hydrogen bonding across the beta-sheet have reduced activity, especially in the presence of physiological concentrations of NaCl. Also, maintaining amphiphilicity of the beta-sheet is key; analogues with substitutions of polar amino acids in the hydrophobic face have reduced activity. Analogues with reduced positive charge tend to be less active, an observation that is more marked for gram-negative than gram-positive bacteria, and may implicate binding to lipopolysaccharide as a key mechanistic step in the killing of gram-negative bacteria. A very large number of amino acid substitutions are tolerated by the protegrin structure, implying that overall structural features such as amphiphilicity, charge, and shape are more important to activity than the presence of specific amino acids. This lack of importance of specific stereochemistry is supported by the fact that completely D-amino acid substituted protegrins are fully potent. Based on the SAR studies, and on the microbiological data from an animal model, one protegrin analogue, IB-367, was selected for clinical development as a topical agent to prevent the oral mucositis associated with cancer therapy.

L6 ANSWER 12 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:352857 BIOSIS
DOCUMENT NUMBER: PREV200000352857
TITLE: Formation and characterization of a single Trp-Trp cross-link in indolicidin that confers protease stability without altering antimicrobial activity.
AUTHOR(S): Osapay, Klara; Tran, Dat; Ladokhin, Alexey S.; White, Stephen H.; Henschen, Agnes H.; Selsted, Michael E. (1)
CORPORATE SOURCE: (1) Dept. of Pathology, College of Medicine, University of California, Irvine, CA, 92697-4800 USA
SOURCE: Journal of Biological Chemistry, (April 21, 2000) Vol. 275, No. 16, pp. 12017-12022. print.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Indolicidin is a 13-residue cationic, **antimicrobial peptide**-amide isolated from the cytoplasmic granules of bovine neutrophils. The unique composition of indolicidin distinguishes it from alpha-helical and beta-structured cationic peptides, because five of indolicidin's 13 residues are tryptophans: H-Ile-Leu-Pro-Trp-Lys-Trp-Pro-Trp-Trp-Pro-Trp-Arg-Arg-NH2. **Solid phase** synthesis of indolicidin gave rise to a minor byproduct that possessed unusual fluorescence and UV absorbance properties compared with authentic

indolicidin. The byproduct was purified by combined ion exchange and reversed phase high pressure liquid chromatography steps and was shown be identical to authentic indolicidin in its microbicidal activity against Staphylococcus aureus, Escherichia coli, Candida albicans, and Cryptococcus neoformans. Mass analysis of the byproduct revealed a 2-atomic mass unit reduction compared with indolicidin, suggesting the deprotonation of two indole side chains to form an intrachain delta1,delta1'-ditryptophan derivative. We confirmed the nature of the cross-linked by-product, termed X-indolicidin, by absorbance and fluoroscence spectroscopy, peptide mapping, and sequence analysis. Edman degradation revealed that Trp-6 and Trp-9 were covalently cross-linked. Compared with indolicidin, X-indolicidin was partially resistant to digestion with trypsin and chymotrypsin, suggesting that the ditryptophan stabilizes a subset of molecular conformations that are protease resistant but that are absent in the native structure.

L6 ANSWER 13 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:331022 BIOSIS
DOCUMENT NUMBER: PREV200000331022
TITLE: Structure-activity relationship study of antimicrobial dermaseptin S4 showing the consequences of peptide oligomerization on selective cytotoxicity.
AUTHOR(S): Feder, Rina; Dagan, Arie; Mor, Amram (1)
CORPORATE SOURCE: (1) Laboratory for Antimicrobial Peptides Investigation, Wolfson Centre for Applied Structural Biology, Hebrew University of Jerusalem, Givat Ram 91904, Jerusalem Israel
SOURCE: Journal of Biological Chemistry, (February 11, 2000) Vol. 275, No. 6, pp. 4230-4238. print.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB To understand how peptide organization in aqueous solution might affect the activity of **antimicrobial peptides**, the potency of various dermaseptin S4 analogs was assessed against human red blood cells (RBC), protozoa, and several Gram-negative bacteria. Dermaseptin S4 had weak antibacterial activity but potent hemolytic or antiprotozoan effects. K4K20-S4 was 2-3-fold more potent against protozoa and RBC, yet K4K20-S4 was more potent by 2 orders of magnitude against bacteria. K4-S4 had similar behavior as K4K20-S4, but K20-S4 and analogous negative charge substitutions were as active as dermaseptin S4 or had reduced activity. Binding experiments suggested that potency enhancement was not the result of increased affinity to target cells. In contrast, potency correlated well with aggregation properties. Fluorescence studies indicated that K20-S4 and all negative charge substitutions were as aggregated as dermaseptin S4, whereas K4-S4 and K4K20-S4 were clearly less aggregated. Overall, the data indicated that N-terminal domain interaction between dermaseptin S4 monomers is responsible for the peptide's oligomerization in solution and, hence, for its limited spectrum of action. Moreover, bell-shaped dose-response profiles obtained with bacteria but not with protozoa or RBC implied that aggregation can have dramatic consequences on antibacterial activity. Based on these results, we tested the feasibility of selectivity reversal in the activity of dermaseptin S4. Tampering with the composition of the hydrophobic domains by reducing hydrophobicity or by increasing the net positive charge affected dramatically the peptide's activity and resulted in various analogs that displayed potent antibacterial activity but reduced hemolytic activity. Among these, maximal antibacterial activity was displayed by a 15-mer version that was more potent by 2 orders of magnitude compared with native dermaseptin S4. These results emphasize the notion that peptide-based antibiotics represent a highly modular synthetic antimicrobial system and provide indications of how the peptide's physico-chemical properties affect potency and selectivity.

L6 ANSWER 14 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:222889 BIOSIS
DOCUMENT NUMBER: PREV200000222889
TITLE: Bactericidal activity of mammalian cathelicidin-derived peptides.
AUTHOR(S): Travis, Sue M.; Anderson, Norma N.; Forsyth, William R.; Espiritu, Cesar; Conway, Barbara D.; Greenberg, E. P.; McCray, Paul B., Jr.; Lehrer, Robert I.; Welsh, Michael J.; Tack, Brian F. (1)
CORPORATE SOURCE: (1) Department of Microbiology, University of Iowa College of Medicine, Bowen Science Building, Iowa City, IA, 52242 USA
SOURCE: Infection and Immunity, (May, 2000) Vol. 68, No. 5, pp. 2748-2755.
ISSN: 0019-9567.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Endogenous **antimicrobial peptides** of the cathelicidin family contribute to innate immunity. The emergence of widespread antibiotic resistance in many commonly encountered bacteria requires the search for new bactericidal agents with therapeutic potential. **Solid-phase** synthesis was employed to prepare linear **antimicrobial peptides** found in cathelicidins of five mammals: human (FALL39/LL37.), rabbit (CAP18), mouse (mCRAMP), rat (rCRAMP), and sheep (SMAP29 and SMAP34). These peptides were tested at ionic strengths of 25 and 175 mM against Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, and methicillin-resistant Staphylococcus aureus. Each peptide manifested activity against P. aeruginosa irrespective of the NaCl concentration. CAP18 and SMAP29 were the most effective peptides of the group against all test organisms under both low- and high-salt conditions. Select peptides of 15 to 21 residues, modeled on CAP18 (37 residues), retained activity against the gram-negative bacteria and methicillin-sensitive S. aureus, although the bactericidal activity was reduced compared to that of the parent peptide. In accordance with the behavior of the parent molecule, the truncated peptides adopted an alpha-helical structure in the presence of trifluoroethanol or lipopolysaccharide. The relationship between the bactericidal activity and several physiochemical properties of the cathelicidins was examined. The activities of the full-length peptides correlated positively with a predicted gradient of hydrophobicity along the peptide backbone and with net positive charge; they correlated inversely with relative abundance of anionic residues. The salt-resistant, antimicrobial properties of CAP18 and SMAP29 suggest that these peptides or congeneric structures have potential for the treatment of bacterial infections in normal and immunocompromised persons and individuals with cystic fibrosis.

L6 ANSWER 15 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:129086 BIOSIS
DOCUMENT NUMBER: PREV200000129086
TITLE: The structure, dynamics and orientation of **antimicrobial peptides** in membranes by multidimensional solid-state NMR spectroscopy.
AUTHOR(S): Bechinger, Burkhard (1)
CORPORATE SOURCE: (1) Max Planck Institute for Biochemistry, Am Klopferspitz 18A, 82152, Martinsried Germany
SOURCE: Biochimica et Biophysica Acta., (Dec. 15, 1999) Vol. 1462, No. 1-2, pp. 157-183.
ISSN: 0006-3002.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Linear peptide antibiotics have been isolated from amphibians, insects and humans and used as templates to design cheaper and more potent analogues for medical applications. Peptides such as cecropins or magainins are

ltoreq40 amino acids in length. Many of them have been prepared by **solid-phase** peptide synthesis with isotopic labels incorporated at selected sites. Structural analysis by solid-state NMR spectroscopy and other biophysical techniques indicates that these peptide antibiotics strongly interact with lipid membranes. In bilayer environments they exhibit amphipathic alpha-helical conformations and alignments of the helix axis parallel to the membrane surface. This contrasts the transmembrane orientations observed for alamethicin or gramicidin A. Models that have been proposed to explain the antibiotic and pore-forming activities of membrane-associated peptides, as well as other experimental results, include transmembrane helical bundles, wormholes, carpets, detergent-like effects or the in-plane diffusion of peptide-induced bilayer instabilities.

L6 ANSWER 16 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:476072 BIOSIS
DOCUMENT NUMBER: PREV199900476072
TITLE: Development and validation of a capillary electrophoresis method for the characterization of protegrin IB-367.
AUTHOR(S): Chen, Jie (1); Fausnaugh-Pollitt, Jodi; Gu, Leo
CORPORATE SOURCE: (1) Pharmaceutical Development Department, IntraBiotics Pharmaceuticals Incorporation, 1245 Terra Bella Avenue, Mountain View, CA, 94043 USA
SOURCE: Journal of Chromatography A, (Aug. 20, 1999) Vol. 853, No. 1-2, pp. 197-206.
ISSN: 0021-9673.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A capillary electrophoresis (CE) method was developed to characterize protegrin IB-367, an **antimicrobial peptide** being developed for the treatment of oral mucositis and for other topical applications. The electrophoretic purity and levels of potential impurities/degradation products of IB-367 drug substance are determined by CE using area normalization. Electrophoresis parameters were optimized to allow optimal resolution, reproducibility and minimal analysis time. The separation and resolution between this polycationic peptide and truncated analogs determined by the CE method was much greater than those by the HPLC methods. In addition, the CE methods separates the potential impurities/degradation products from each other while the HPLC methods failed to resolve them. The CE method was validated in the aspects of accuracy, precision, linearity, range, limit of detection, limit of quantitation, specificity, system suitability and robustness. An internal standard was used for the quantitation purpose. The selection criteria of the internal standard as well as the method validation results are presented. The truncated peptide analogs were used to demonstrate the specificity of the method. These analogs were also used to evaluate the limit of quantitation of potential impurities. The relative response factors of these analogs were assessed to determine area normalization feasibility. System suitability tests were established.

L6 ANSWER 17 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:475402 BIOSIS
DOCUMENT NUMBER: PREV199800475402
TITLE: Structure-activity analysis of brevinin 1E amide, an **antimicrobial peptide** from Rana esculenta.
AUTHOR(S): Kwon, Mi-Yun; Hong, Sung-Yu; Lee, Keun-Hyeung (1)
CORPORATE SOURCE: (1) Protein Chem. Lab., Mogam Biotechnol. Res. Inst., 341 Pojung-Ri, Koosung-Myun, Yongin-City, Kyunggi-Do 449-910 South Korea
SOURCE: Biochimica et Biophysica Acta, (Sept. 8, 1998) Vol. 1387, No. 1-2, pp. 239-248.
ISSN: 0006-3002.
DOCUMENT TYPE: Article

LANGUAGE: English

AB Brevinin 1E, consisting of 24 amino acid residues, from Rana esculenta has potent antimicrobial and hemolytic activity. From a structural point of view, this peptide has a N-terminal hydrophobic region, a proline hinge region in the middle and a C-terminal loop region delineated by an intra-disulfide bridge, which is a common structural feature of **antimicrobial peptides** from Rana species. To investigate the structural features for antimicrobial and hemolytic activity, truncated and linearized brevinin 1E amides were synthesized and characterized. A deletion of three amino acids from the N-terminal region did not greatly affect antimicrobial activity but dramatically reduced hemolytic activity. The contribution of the intra-disulfide bridge to antimicrobial and hemolytic activity was somewhat different between brevinin 1E amide and truncated fragments. In brevinin 1E amide, the elimination of the intra-disulfide bridge did not greatly affect antimicrobial and hemolytic activity whereas the elimination of the intra-disulfide bridge in the truncated fragments did not decrease antimicrobial activity but did decrease hemolytic activity. Circular dichroism spectra and the retention time on the C18 reverse phase column revealed that the intra-disulfide bridge (i, i+6) formed an amphipathic loop which increased hydrophobicity and helped to induce the alpha-helical structure in the membrane-mimetic environment. Even though the intra-disulfide bridge and the N-terminal region were responsible for the alpha-helical structure and hydrophobicity, these two structural features were not essential for antimicrobial activity. The hemolytic activity of brevinin 1E amide and its analogs also correlated well with the retention time rather than the alpha-helicity.

L6 ANSWER 18 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:342021 BIOSIS
DOCUMENT NUMBER: PREV199800342021
TITLE: Structure, synthesis, and molecular cloning of dermaseptins B, a family of skin peptide antibiotics.
AUTHOR(S): Charpentier, Stephane; Amiche, Mohamed; Mester, Jan; Vouille, Veronique; Le Caer, Jean-Pierre; Nicolas, Pierre; Delfour, Antoine (1)
CORPORATE SOURCE: (1) Lab, Bioactivation Peptides, Inst. Jacques Monod, Univ. Paris 7, 2 Place Jussieu, 75251 Paris Cedex 05 France
SOURCE: Journal of Biological Chemistry, (June 12, 1998) Vol. 273, No. 24, pp. 14690-14697.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Analysis of antimicrobial activities that are present in the skin secretions of the South American frog Phyllomedusa bicolor revealed six polycationic (lysine-rich) and amphipathic alpha-helical peptides, 24-33 residues long, termed dermaseptins B1 to B6, respectively. Prepro-dermaseptins B all contain an almost identical signal peptide, which is followed by a conserved acidic propiece, a processing signal Lys-Arg, and a dermaseptin progenitor sequence. The 22-residue signal peptide plus the first 3 residues of the acidic propiece are encoded by conserved nucleotides encompassed by the first coding exon of the dermaseptin genes. The 25-residue amino-terminal region of prepro-dermaseptins B shares 50% identity with the corresponding region of precursors for D-amino acid containing opioid peptides or for **antimicrobial peptides** originating from the skin of distantly related frog species. The remarkable similarity found between prepro-proteins that encode end products with strikingly different sequences, conformations, biological activities and modes of action suggests that the corresponding genes have evolved through dissemination of a conserved "secretory cassette" exon.

L6 ANSWER 19 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:208148 BIOSIS
DOCUMENT NUMBER: PREV199800208148

TITLE: Cecropin A-melittin hybrid peptide exerts its antifungal effects by damaging on the plasma membranes of Trichosporon beigelii.
AUTHOR(S): Lee, Dong Gun; Shin, Song Yub; Maeng, Cheol-Young; Hahm, Kyung-Soo (1)
CORPORATE SOURCE: (1) Peptide Eng. Res. Unit, Kor. Res. Inst. Biosci. Biotechnol., P.O. Box 115, Yusong, Taejon 305-600 Korea
SOURCE: Biotechnology Letters, (March, 1998) Vol. 20, No. 3, pp. 211-214.
ISSN: 0141-5492.
DOCUMENT TYPE: Article
LANGUAGE: English
AB To elucidate the effect of the peptide derived from cecropin A(1-8)-melittin(1-12) having potent antifungal activity without cytotoxicity against eukaryotic cell on the fungal cell membranes, Trichosporon beigelii protoplasts were prepared. The protoplasts treated with the peptide not only failed to regenerate the fungal cell walls but also disrupted the membrane, indicating that the peptide exerts its antifungal activity by acting on the plasma membranes.

L6 ANSWER 20 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:250302 BIOSIS
DOCUMENT NUMBER: PREV199799549505
TITLE: Chemoattractant properties of PR-39, a neutrophil antibacterial peptide.
AUTHOR(S): Huang, Hsuan-Jen; Ross, Christopher R.; Blecha, Frank (1)
CORPORATE SOURCE: (1) Dep. Anat. and Physiol., VMS 228, 1600 Denison Ave., Kans. State Univ., Manhattan, KS 66506-5602 USA
SOURCE: Journal of Leukocyte Biology, (1997) Vol. 61, No. 5, pp. 624-629.
ISSN: 0741-5400.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The proline-arginine (PR)-rich antibacterial peptide, PR-39, kills bacteria by a non-pore-forming mechanism. Because this neutrophil peptide possesses several distinct functional properties and because other **antimicrobial peptides** are chemoattractants, we sought to determine whether PR-39 was a chemoattractant for porcine leukocytes. The peptide was synthesized by the **solid-phase** method using t-Boc chemistry and purified by reversed-phase highperformance liquid chromatography. Leukocyte migration was assessed with the use of a 48-well micro-chemotaxis chamber. PR-39 induced the directed migration of neutrophils. The peak chemotaxis response occurred at 0.5-2 mu-M, which was slightly lower than the minimal inhibitory and bactericidal concentrations for PR-39. However, the peptide was not a chemoattractant for mononuclear cells. Truncation of PR-39 suggested that the neutrophil chemoattractant domain may be contained within the first 26 amino acid residues. Intracellular Ca-2+ fluxes in response to PR-39 were monitored by flow cytometry and showed a transient increase that peaked at approximately 40 s and approached basal values by 4 min. However, in a Ca-2+-free environment, the PR-39-induced Ca-2+ increase was abrogated. Furthermore, PR-39 did not induce neutrophil chemotaxis in the absence of extracellular Ca-2+, and pertussis toxin inhibited both neutrophil chemotaxis and Ca-2+ mobilization. Taken together, these data suggest that PR-39 is a Ca-2+-dependent chemoattractant of neutrophils. The finding of a neutrophil antibacterial peptide that is also a neutrophil chemoattractant is intriguing and may indicate an important role for PR-39 in inflammation.

L6 ANSWER 21 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:83840 BIOSIS
DOCUMENT NUMBER: PREV199799375553
TITLE: Antibacterial activities of peptides designed as hybrids of **antimicrobial peptides**.
AUTHOR(S): Shin, Song Yub; Kang, Joo Hyun; Lee, Myung Kyu; Hahm,

Kyung-Soo (1)
CORPORATE SOURCE: (1) Peptide Eng. Res. Unit, Korea Res. Inst. Biosci. Biotechnol., KIST, P.O. Box 115, Taejon 305-600 South Korea
SOURCE: Journal of Biochemistry and Molecular Biology, (1996) Vol. 29, No. 6, pp. 545-548.
ISSN: 1225-8687.
DOCUMENT TYPE: Article
LANGUAGE: English
AB CA(1-8)ME(1-12), the CA-ME hybrid peptide of the amino terminal segments of cecropin A (CA) and melittin (ME). has been reported to have a broad spectrum and improved potency without a hemolytic property. In order to obtain new synthetic peptides with powerful antibacterial activity without hemolytic activity. several hybrid peptides were designed from the sequences of CA. ME, magainin 2, bombinin and lactoferricin. All hybrid peptides were constructed to form an amphipathically basic-flexible-hydrophobic structure and synthesized by the **solid phase** method. Their hemolytic activities against human red blood cells and antibacterial activities against both Gram-positive and Gram-negative bacteria were determined. CA(18)MA(1.12), CA(1-8)BO(1-12). MA(10-17)ME(1-12) and LF(20-29)ME(1-12) showed comparable activities with broad spectra against both Gram-positive and Gram-negative bacteria relative to CA(1-8)ME(1-12) but without hemolytic properties. These hybrid peptides, therefore, could be useful as model peptides to design a novel peptide with improved antibacterial activity and study on structure-activity relationships of **antimicrobial peptides**.

L6 ANSWER 22 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:338429 BIOSIS
DOCUMENT NUMBER: PREV199699060785
TITLE: Covalent structure, synthesis, and structure-function studies of mesentericin Y 105-37, a defensive peptide from Gram-positive bacteria Leuconostoc mesenteroides.
AUTHOR(S): Fleury, Yannick; Dayem, Manal Abdel; Montagne, Jean Jacques; Chaboisseau, Eddy; Pierre Le Caer, Jean; Nicolas, Pierre; Delfour, Antoine (1)
CORPORATE SOURCE: (1) Laboratoire de Biochimie des Proteines, I.B.M.I.G., Universite de Poitiers, 40 Avenue du Recteur Pineau, 86022 Poitiers Cedex France
SOURCE: Journal of Biological Chemistry, (1996) Vol. 271, No. 24, pp. 14421-14429.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
AB A 37-residue cationic **antimicrobial peptide** named mesentericin Y 105-37 was purified to homogeneity from cell-free culture supernatant of the Gram-positive bacterium Leuconostoc mesenteroides. The complete amino acid sequence of the peptide, KYYGNGVHCTKSGCSVNWGEAASAGIHRL ANGGNGFW, has been established by automated Edman degradation, mass spectrometry, and **solid phase** synthesis. Mesentericin Y 105-37 contains a single intramolecular disulfide bond that forms a 6-membered ring within the molecule. Mesentericin Y 105-37 was synthesized by the **solid phase** method. The synthetic replicate was shown to be indistinguishable from the natural peptide with respect to electrophoretic and chromatographic properties, mass spectrometry analysis, automated amino acid sequence determination, and antimicrobial properties. At nanomolar concentrations, synthetic mesentericin Y 105-37 is active against Gram+ bacteria in the genera Lactobacillus and Carnobacterium. Most interestingly, the peptide is inhibitory to the growth of the food-borne pathogen Listeria. CD spectra of mesentericin Y 105-37 in low polarity medium, which mimic the lipophilicity of the membrane of target organisms, indicated 30-40% alpha-helical conformation, and predictions of secondary structure suggested that the peptide can be configured as an amphipathic helix spanning over residues 17-31. To reveal the molecular basis of the specificity of mesentericin Y 105-37 targeting

and mode of action, NH-2- or COOHterminally truncated analogs together with point-substituted analogs were synthesized and evaluated for their ability to inhibit the growth of Listeria ivanovii. In sharp contrast with broad spectrum alpha-helical **antimicrobial peptides** from vertebrate animals, which can be shortened to 14-18 residues without deleterious effect on potency, molecular elements responsible for anti-Listeria activity of mesentericin Y 105-37 are to be traced at once to the NH-2-terminal tripeptide KYY, the disulfide bridge, the putative alpha-helical domain 17-31, and the COOH-terminal tryptophan residue of the molecule. It is proposed that the amphipathic helical domain of the peptide interacts with lipid bilayers, leading subsequently to alteration of the membrane functions, whereas residues 1-14 form part of a recognition structure for a membrane-bound receptor, which may be critical for peptide targeting. Because mesentericin Y105-37 is easy to synthesize at low cost, it may represent a useful and tractable tool as a starting point for the design of more potent analogs that may be of potential applicability in foods preservation.

L6 ANSWER 23 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:298868 BIOSIS
DOCUMENT NUMBER: PREV199598313168
TITLE: Synthesis and characterization of indolicidin, a tryptophan-rich **antimicrobial peptide** from bovine neutrophils.
AUTHOR(S): Van Abel, Robert J.; Tang, Yi-Quan; Rao, V. S. V.; Dobbs, Craig H.; Tran, Dat; Barany, George (1); Selsted, Michael E.
CORPORATE SOURCE: (1) Dep. Chem., Univ. Minnesota, 207 Pleasant St. SE, Minneapolis, MN 55455 USA
SOURCE: International Journal of Peptide & Protein Research, (1995) Vol. 45, No. 5, pp. 401-409.
ISSN: 0367-8377.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Indolicidin, a novel tryptophan-rich microbicidal tridecapeptide amide isolated originally from granules of bovine neutrophils, has been prepared by optimized manual and automated protocols of stepwise **solid-phase** synthesis with N-alpha-9-fluorenylmethyloxycarbonyl (Fmoc) amino acid derivatives. Both standard polystyrene (PS) and polyethylene glycol-polystyrene (PEG-PS) graft supports were used in combination with handles that provide C-terminal peptide amides: 5-(4-Fmoc-aminomethyl-3,5-dimethoxyphenoxy)valeric acid (PAL) or 5-(9-Fmoc-aminoxanthen-2-oxy)valeric acid (XAL). Final deprotection/cleavage was carried out with reagent K, trifluoroacetic acid-phenol-water-thioanisole-1,2-ethanedithiol (82.5:5:5:5:2.5), or reagent B, trifluoroacetic acid-phenol-water-tri(isopropyl)silane (88:5:5:2), and related cocktails. Initial purities as high as 93% were obtained immediately following cleavage. In the largest-scale synthesis carried out, 0.8 g of HPLC-purified indolicidin ( gt 99% pure) was obtained, representing a 39% overall yield based on C-terminal Arg(Pmc) anchored to PAL-PS-resin. The main synthetic product, and some by-products, were characterized by analytical high-performance liquid chromatography (HPLC), sequencing, and fast atom bombardment mass spectrometry (FABMS). The antimicrobial potencies of natural and synthetic indolicidin, as determined by in vitro antibacterial and antifungal assays, were identical. Further, the reactivities of natural and synthetic peptides with anti-indolicidin antibody were indistinguishable.

L6 ANSWER 24 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:154099 BIOSIS
DOCUMENT NUMBER: PREV199598168399
TITLE: Antimicrobial activities of amphiphilic peptides covalently bonded to a water-insoluble resin.
AUTHOR(S): Haynie, Sharon L. (1); Crum, Grace A.; Doele, Bruce A.
CORPORATE SOURCE: (1) Central Res. and Development, E.I. DuPont de Nemours and Co., Experimental Stn., P.O. Box 80328, Wilmington, DE

19880-0328 USA
SOURCE: Antimicrobial Agents and Chemotherapy, (1995) Vol. 39, No. 2, pp. 301-307.
ISSN: 0066-4804.
DOCUMENT TYPE: Article
LANGUAGE: English
AB A series of polymer-bound **antimicrobial peptides** was prepared, and the peptides were tested for their antimicrobial activities. The immobilized peptides were prepared by a strategy that used **solid-phase** peptide synthesis that linked the carboxy-terminal amino acid with an ethylenediamine-modified polyamide resin (PepsynK). The acid-stable, permanent amide bond between the support and the nascent peptide renders the peptide resistant to cleavage from the support during the final acid-catalyzed deprotection step in the synthesis. Select immobilized peptides containing amino acid sequences that ranged from the naturally occurring magainin to simpler synthetic sequences with idealized secondary structures were excellent antimicrobial agents against several organisms. The immobilized peptides typically reduced the number of viable cells by gtoreq 5 log units. We show that the reduction in cell numbers cannot be explained by the action of a soluble component. We observed no leached or hydrolyzed peptide from the resin, nor did we observe any antimicrobial activity in soluble extracts from the immobilized peptide. The immobilized peptides were washed and reused for repeated microbial contact and killing. These results suggest that the surface actions by magainins and structurally related **antimicrobial peptides** are sufficient for their lethal activities.

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